

PCBs: ICF Status Report

December 3rd, 2020



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Action Items

Topic	Task	Assigned to	Date Due	Slide #
Epi neuro study evaluation	Full Team Meeting for Batch 9	ICF	12/3/2020	5
Epi neuro study evaluation	Complete Batch 10 review	ICF	12/18/2020	5
Epi neuro study evaluation	EPA to send HERO IDs to ICF for Batch 11	EPA (Geniece)	12/11/2020	5
2020 Literature Update	Full-text screening – revise instructions and prepare screening/extraction forms	ICF (Cynthia)	12/18/2020	7
Evidence Map Manuscript	Contact expert authors about outstanding drafts and revisions	ICF (Raquel)	Ongoing	8
Evidence Map Manuscript	EPA to provide feedback on revised drafts.	EPA (Geniece)	Ongoing	8
Half-Lives manuscript	Complete text analytics screen and data extraction	ICF (Joanne)	1/29/2021	10
ADME	Complete Extractions of 77 Additional Step 3 Studies	ICF (Steven)	12/23/2020	4
ADME	Update Literature Flow Diagram	ICF (Raquel)	12/30/2020	4
ADME Inventories	Joanne to schedule meeting with Paul Schlosser.	ICF (Joanne)	TBD	11
MiST – Tool and User Guide	EPA to review tool and User Guide	EPA	-	4
MiST - Presentation	Waiting for EPA review of MiST and the User Guide	ICF (Joanne)	-	4
Management	Prepare workplan for TO-34/TD-005, TD-006	ICF (Raquel)	12/11/2020	12



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Major Decisions

TO-37

- * **Management**
 - ... No new major decisions.
- * **HAWC Study Evaluations and Data Extractions**
 - ... No new major decisions.
- * **2020 Literature Update**
 - ... No new major decisions.

TO-34

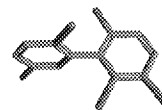
- * **Management**
 - ... Considering the budgets for TD-005 and TD-006, the overall TO-34 budget will be committed to all active TDs and management tasks. Any additional TDs may need to be considered for the next POP, unless funding becomes available.
- * **Half-Lives Manuscript**
 - ... ICF to conduct data extraction.
- * **ADME**
 - ... 53 studies found in Hazard ID will not be used as seeds. The old seeds will be re-used but these 53 studies will be screened first to help the machine learning model develop.
 - ... ICF will prepare a single literature flow diagram, including an explanation for use of DoCTER and SWIFT pre- and post-2019, respectively.
 - ... ADME Inventories will be transitioned to litstream™ and new inventory work will be conducted in litstream™.



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Agenda for December 3rd, 2020



§ TO-37/TD-003

- § Study evaluation
- § HAWC extractions
- § 2020 Literature update

* TO-34 + TO-09/TD-003

- * Evidence Map Manuscript (TO-34/TD-001, TO-09/TD-003)
- * Half-lives Manuscript (TO-34/TD-004)
- * ADME Inventories (TO-34/TD-005)

Quick updates:

- * TO-09/TD-008
 - Analysis of Co-eluting PCBs
- * ADME
 - ADME lit flow diagram – in preparation (all studies vs pre-2019 + 2019?)
 - Step 3 – 77 additional studies – resumed; revised report due 12/18/2020
 - MiST – waiting for EPA feedback
 - TD-006 – work plan in preparation; 2020 Hazard ID screen - 53 studies tagged to ADME



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Co-Eluting PCBs

The new search seen in HERO is a sub project that will be tagged to its own project, not attached to the main PCBs project. No action is needed from ICF, EPA will correct the tags.

ADME Lit flow diagram

ICF will prepare a single literature flow diagram, including an explanation for use of DoCTER and SWIFT pre- and post-2019, respectively.

ADME Step 3 – 77 Studies

No Comments

MiST

EPA will provide feedback

TD-006 Work Plan

In preparation, will be finalized after the workplan for TD-005 is finalized, as they are dependent on each other.

For the 53 studies found, we could screen them and use the relevant ones as seeds, we could also use the same seeds from last year

From a documentation standpoint, it would be simpler to just use the same seeds as last year.

Decision: 53 studies found in Hazard ID will not be used as seeds. The old seeds will be re-used but these 53 studies will be screened first to help the machine learning model develop.

WP is expected to be delivered next week.

Literature screening & developing inventories

■ TO-37/TD-003 revised work plan (v4) under internal ICF review

- Task 1 – two additional neurotox batches (14 studies)
- Task 2 – data extraction for human studies (10 batches)

■ Task 1: Study evaluation

■ Epi neuro studies

- Batch 9 – ICF reviews completed 12/1. Full team meeting scheduled for 12/3.
- Batch 10 - Sharon and Pradeep's preview is due 12/4. ICF assignments will be made on 12/7 and will be completed by 12/18. Full team meeting is scheduled for January 7.
- Batch 11 – Geniece to send HERO IDs to ICF on 12/11, and ICF to send on to Sharon and Pradeep on 12/14.

■ Neurotox studies

- Batch 7A – Full team review meeting held on 11/20
- Batches 8A and 9A – not started (waiting for submission and approval of revised workplan)



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Literature screening & developing inventories

■ Task 2: Data extraction

■ Epi neuro studies (TD-003 Addendum 3, 10 batches, ~90 studies total)

- Expected start in January (Batch 1 initial expert review)
- Batch 2 will only start after Batch 1 is finalized

■ Tox neuro studies (8 batches, ~40 studies total)

- Batch 1
 - ICF concluded extractions QC on 11/24, corrections/clarifications submitted on 12/1
- Batch 2
 - Not started

■ Task 3: Reference tagging in litstream and HERO

- No changes

■ Task 4: Update documentation and literature flow diagram

- No changes



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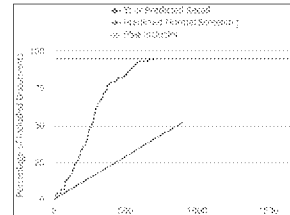
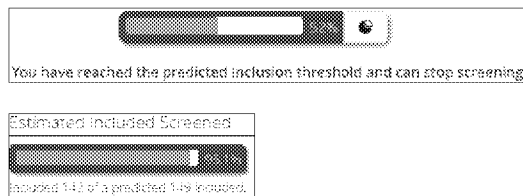
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Literature screening & developing inventories

■ Task 5: 2020 Literature Update

- **Literature search update** (COMPLETED, 1764 Unique Results)
- **Title/abstract screening** (COMPLETED)
 - 897 (52% of 1725) screened in SWIFT Active Screener to capture 95% of the predicted number of included studies. 142 included studies will move onto full-text screening in litstream™.

Level	Cumulative Included		Partially Screened	Not Screened	Not Screened	Total
	Screened	Excluded				
Level 1 - Title & Abstract	142	752	0	8	828	1725



» Title-only references (n=29) screened in litstream™ (in progress)

- **Setting up data and forms in litstream™ for full text screening/extraction**



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Evidence Map Manuscript – Draft Sections Progress

Health Effect Category	Assigned to	Status
Cardiovascular	Alexander Sergeev (epi), Michal Toborek (tox)	Alex and Michal met on 11/30. Revised draft in prep. (ETC: 12/18)
Dermal	Robyn Blain	Final draft (completed)
Developmental	John Meeker (epi), Aileen Keating (tox)	EPA provided feedback on revised draft on 11/20. Waiting for response.
Endocrine	Michael Bloom (epi), Joanne Trgovcich (tox)	EPA provided feedback on 11/23. Revised draft in prep. (ETC: 12/18)
Gastrointestinal	Evan Coffman (epi), Brandall Ingle / Joanne Trgovcich (tox)	Final draft (completed)
Hepatobiliary	Evan Coffman (epi), Larry Robertson (tox)	Final revision in progress.
Immunological	Todd Jusko (epi), Geniece Lehmann (tox)	Epi outline/draft in progress (ETC: 11/25)
Metabolic	Alexander Sergeev (epi), Michal Toborek (tox)	EPA combining Epi and Tox inputs.
Musculoskeletal	Cynthia Lin (epi), Kelly Shipkowski (tox)	EPA provided feedback on revised draft on 11/20. ICF revising draft (ETC: 12/11)
Neurological	Pradeep Rajan & Sharon Sagiv (epi), Pam Lein & Carrie Klocke (tox)	EPA provided feedback on 10/1. Revised draft in progress (ETC: 12/23?)
Ocular	Robyn Blain	Final draft to be revised given new studies in inventory
Reproductive	Pam Factor-Litvak (epi) Erin Yost (tox), Xabier Arzuaga (tox)	Reviewed Epi draft – male and Epi outline - female submitted on 10/27 – Pam to review revised draft?
Respiratory	Raquel Silva (epi), Samantha Snow (tox)	Final draft to be revised given new studies in inventory



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Half-lives Manuscript: KAT Search Results on Literature from 2019 – 2020

KAT Search - 2019 and 2020 Literature	Count
Total Documents Retrieved	3501
Documents with No Keywords Other Source	2690
Documents with One or More Keywords	811
Documents with No Keywords PubMed Source	0

Result	Count	Percentage
documents with one or more keywords	811	100
off topic	47	6
on topic	796	98
eco terms*	348	43

*43.7% of on topic

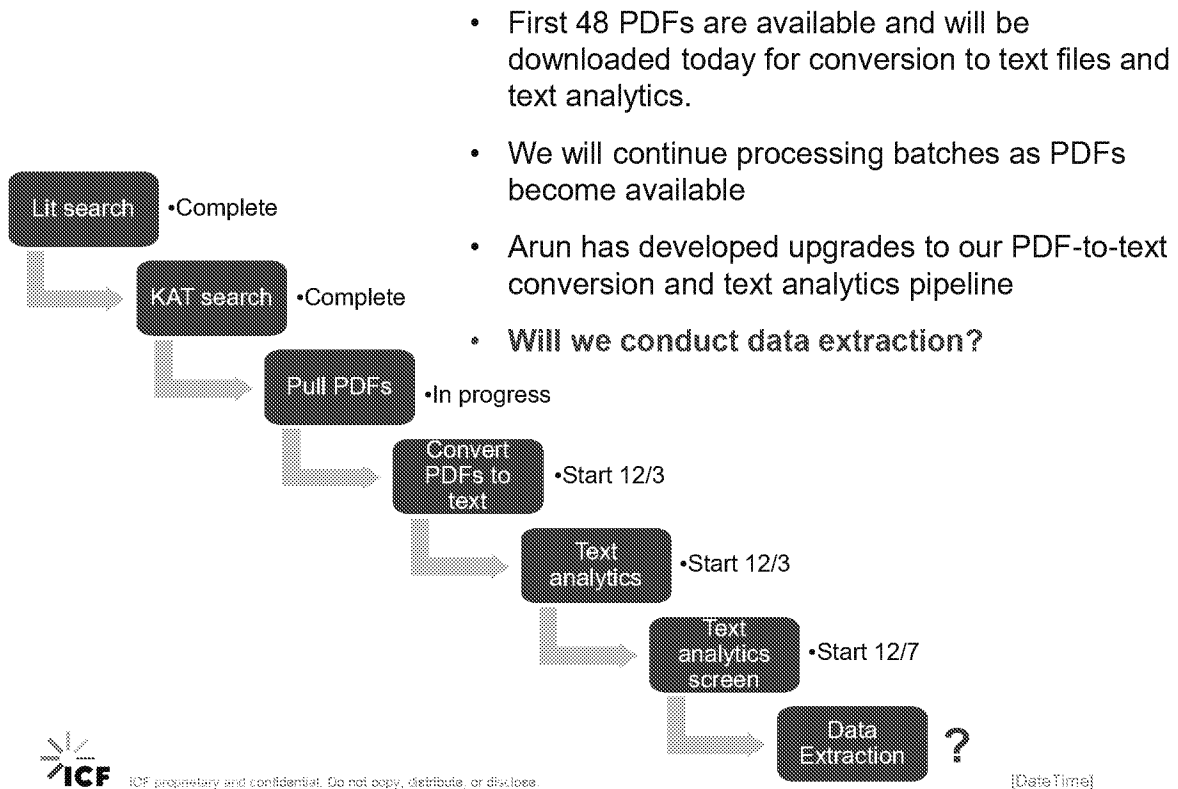


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Work plan may need to be revised if the number of studies to be extracted is larger than planned

KAT Search: Timeline, Progress, and Questions



ICF will be conducting the data extractions. ICF will begin training next week.

ADME Inventory Update

- **Work plan in preparation**
- **Estimated Number of Studies to Extract**

Year	Estimated Count
2019*	248

*179 currently eligible for inventories plus estimating 90% of the 77 additional studies will move to inventories

- **Excel or Litstream?** ICF estimates it may take ~40 hrs to generate FlexForms for human, animal and in vitro inventories, upload existing inventories into litstream, and develop reports from litstream to match existing inventory structure.

Subtask	Hours
FlexForms and litstream instructions	20
Upload existing reports	16
Generate scripts for reports	4
Total	40



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Joanne has requested that we meet with Paul to review the inventories and ensure the proper inventories are prepared. Joanne to schedule this meeting.

ICF litstream team estimates about 40 hours to move the inventories to litstream

These hours were included in the budget estimates discussed in slide 13

ADME Inventories will be transitioned to litstream and new inventory work will be conducted in litstream. This will be included in the work plan.

Budget, as of 11/27/2020

TO/TD	Budget Hours	Budget \$	Current Hours	Current \$	Cumul. Hours	Cumul. \$	Remain. Hours	Remain. \$
TO-34							66%	64%
Total								
Tasks 1&2								
TD-001 (EM)								
TD-002 (ADME), v3								
TD-003 (MiST), v2								
TD-004 (Half-lives), v1								
TO-37								
TD-003 (WP v3)								

Ex. 4 CBI

* TO-34:

- * TD-001 – Workplan v2 approved on 7/31
- * TD-002 – Workplan v3 submitted and approved on 11/24
- * TD-003 – Workplan v2 approved on 10/27
- * TD-004 – Workplan v1 approved on 11/12
- * TD-005, TD-006 – Workplans in preparation

* TO-37/TD-003

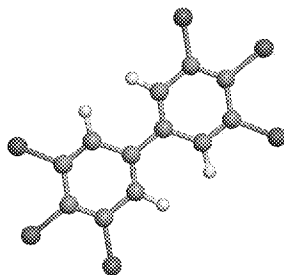
- * Workplan (v1), approved on 7/10
- * Addendum received on 8/5, WP (v2) approved on 9/22
- * Addendum 2 received on 9/18, WP (v3) approved on 10/5
- * WP (v4) under internal ICF review
 - ... Task 1 – 2 additional batches, ~14 neurotox studies
 - ... Task 2 – 10 additional batches, ~90 neuro epi studies (Addendum 3)



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Considering the budgets for TD-005 and TD-006, the overall TO-34 budget will be committed to all active TDs and management tasks. Any additional TDs may need to be considered for the next POP, unless funding becomes available.



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